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NEWS
NEWS
         NOV 21
                 CAS patent coverage to include exemplified prophetic
                 substances identified in English-, French-, German-,
                 and Japanese-language basic patents from 2004-present
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         NOV 26
                 MARPAT enhanced with FSORT command
NEWS
         NOV 26
                 CHEMSAFE now available on STN Easy
         NOV 26
NEWS
                 Two new SET commands increase convenience of STN
                 searching
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         DEC 01
                 ChemPort single article sales feature unavailable
      6
                 GBFULL now offers single source for full-text
NEWS
         DEC 12
                 coverage of complete UK patent families
NEWS
      8
         DEC 17
                 Fifty-one pharmaceutical ingredients added to PS
NEWS
         JAN 06
                 The retention policy for unread STNmail messages
                 will change in 2009 for STN-Columbus and STN-Tokyo
                 WPIDS, WPINDEX, and WPIX enhanced Japanese Patent
NEWS 10
         JAN 07
                 Classification Data
                 Simultaneous left and right truncation (SLART) added
NEWS 11 FEB 02
                 for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
NEWS 12 FEB 02
                 GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 13 FEB 06
                 Patent sequence location (PSL) data added to USGENE
NEWS 14 FEB 10 COMPENDEX reloaded and enhanced
NEWS 15 FEB 11
                 WTEXTILES reloaded and enhanced
NEWS 16
         FEB 19
                 New patent-examiner citations in 300,000 CA/CAplus
                 patent records provide insights into related prior
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         FEB 19
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                 terms from the IPC Thesaurus, Version 2009.01
NEWS 18
         FEB 23
                 Several formats for image display and print options
                 discontinued in USPATFULL and USPAT2
         FEB 23
                 MEDLINE now offers more precise author group fields
NEWS 19
                 and 2009 MeSH terms
NEWS 20
         FEB 23
                 TOXCENTER updates mirror those of MEDLINE - more
                 precise author group fields and 2009 MeSH terms
NEWS 21
         FEB 23
                 Three million new patent records blast AEROSPACE into
                 STN patent clusters
NEWS 22
         FEB 25
                 USGENE enhanced with patent family and legal status
                 display data from INPADOCDB
                 INPADOCDB and INPAFAMDB enhanced with new display
NEWS 23
         MAR 06
                  formats
                 EPFULL backfile enhanced with additional full-text
NEWS 24
         MAR 11
                 applications and grants
NEWS 25
         MAR 11
                 ESBIOBASE reloaded and enhanced
NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
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AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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STRUCTURE FILE UPDATES: 11 MAR 2009 HIGHEST RN 1119363-64-2 DICTIONARY FILE UPDATES: 11 MAR 2009 HIGHEST RN 1119363-64-2

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http://www.cas.org/support/stngen/stndoc/properties.html

=> s lamotrigine/cn 1 LAMOTRIGINE/CN L1

=> d str cn rn

ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

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H<sub>2</sub>N NH<sub>2</sub> Cl
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# \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (CA INDEX NAME) OTHER NAMES:

CN 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine

CN 6-(2,3-Dichlorophenyl)-1,2,4-triazine-3,5-diamine

CN BW 430C

CN Lamictal

CN Lamictal XR

CN Lamotrigin

CN Lamotrigine

CN LTG

RN 84057-84-1 REGISTRY

=> file caplus medline biosis embase

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 8.36 8.58

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 10:18:09 ON 12 MAR 2009
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=> s 84057-84-1

L2 17000 84057-84-1

=> s lamotrigine

L3 18579 LAMOTRIGINE

=> s L2 or L3

L4 18655 L2 OR L3

=> s multiple sclerosis

L5 133765 MULTIPLE SCLEROSIS

=> s L4 and L5

L6 269 L4 AND L5

=> dup rem L6

PROCESSING COMPLETED FOR L6

L7 228 DUP REM L6 (41 DUPLICATES REMOVED)

=> s L7 and (AY<2004 or PY<2004 or PRY<2004)

'2004' NOT A VALID FIELD CODE

L8 76 L7 AND (AY<2004 OR PY<2004 OR PRY<2004)

# => d 1-10 L8 ibib abs

L8 ANSWER 1 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:1156137 CAPLUS

DOCUMENT NUMBER: 149:409732

TITLE: Pharmaceutical compositions and method for treatment

of chronic inflammatory diseases

INVENTOR(S): Shapiro, Howard K.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 35pp., Cont.-in-part of U.S.

Ser. No. 924,945.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20080234380	A1	20080925	US 2008-70518	20080220 <
US 20050090553	A1	20050428	US 2004-924945	20040824 <
PRIORITY APPLN. INFO.:			US 1992-906909 E	32 19920630 <
			US 1994-241603 E	32 19940511 <
			US 1997-814291 E	32 19970310 <
			US 2000-610073 E	32 20000705 <
			US 2004-924945	2 20040824

AΒ This invention defines novel compns. that can be used for clin. treatment of a class of chronic inflammatory diseases. Increased generation of carbonyl substances, namely aldehydes and ketones, occurs at sites of chronic inflammation and is common to the etiologies of all of the clin. disorders addressed herein. Such carbonyl substances are cytotoxic and addnl. serve to perpetuate and disseminate the inflammatory process. This invention defines use of compns., the orally administered required primary agents of which are primary amine derivs. of benzoic acid capable of covalently reacting with the carbonyl substances. P-Aminobenzoic acid is an example of the required primary agent of the present invention. PABA has a small mol. weight, is water-soluble, has a primary amine group which reacts with carbonyl-containing substances and is tolerated by the body in relatively high dosages for extended periods. The method includes administration of a composition comprising: (1) an orally consumed therapeutically effective amount of at least one required primary agent; (2) at least one required previously known medicament co-agent recognized as effective to treat a chronic inflammatory disease addressed herein administered to the mammalian subject via the oral route; and (3) one or more addnl. orally consumed required co-agent selected from the group consisting of antioxidants, vitamins, metabolites at risk of depletion, sulfhydryl co-agents, co-agents which may facilitate glutathione activity and nonabsorbable primary amine polymeric co-agents; so as to-produce an additive or synergistic physiol. effect of an anti-inflammatory nature.

DOCUMENT NUMBER: 143:172866

TITLE: Preparation of isothiazole dioxides as CXC- and

CC-chemokine receptor ligands

INVENTOR(S): Taveras, Arthur G.; Zheng, Junying; Biju, Purakkattle

J.; Yu, Younong; Chao, Jianhua; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J.

Robert; Baldwin, John J.; Lai, Gaifa; Wu, Minglang

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug

Discovery, Inc.

SOURCE: PCT Int. Appl., 427 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

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CN	1918	156			Α		2007	0221		CN 2	004-	8004	1794		2	0041	220	<
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OTHER S	OURCE	(S):			CASI	REAC	Т 14	3:17	2866	; MA	RPAT	143	:172	866				

# \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Disclosed are novel compds. I [D, E = N, CR50; provided that D and E are not the same (one is N and the other is CR50); R50 = H, CF3, CN, etc.; A = (hetero)aryl, (hetero)arylalkyl; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and cardiac reperfusion injury, pain (e.g., acute pain, acute and chronic inflammatory pain, and neuropathic pain) using a compound I. Although the methods of preparation are not claimed, hundreds of example prepns. and/or characterization data are included. For example, II was prepared in 68% yield from the isothiazoledioxide III and the amine IV.pTSA (preparation of reactants given). Antagonist activities of some

examples of I towards CXCR1, CXCR2 and CCR7 are given.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:638859 CAPLUS

DOCUMENT NUMBER: 143:153384

TITLE: Preparation of diaminothiadiazoles as CXC- and

CC-chemokine receptor ligands

INVENTOR(S): Biju, Purakkattle J.; Taveras, Arthur G.; Yu, Younong;

Zheng, Junying; Chao, Jianhua; Aki, Cynthia J.; Fine,

Jay; Lundell, Daniel; Priestley, Tony; Reggiani,

Angelo; Merritt, J. Robert; Baldwin, John J.

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug

Discovery, Inc.

SOURCE: PCT Int. Appl., 593 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA:	TENT	NO.					DATE				ICAT					ATE		
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											004-				A3 2			
										wO 2	004-	US42	U6U		W 2	0041	Z16	

OTHER SOURCE(S): MARPAT 143:153384

GΙ

AB Disclosed are diaminothiadiazoles I [A = (hetero)aryl, (hetero)arylmethyl (substituted at CH2), etc.; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and ischemia reperfusion injury, acute pain, acute and chronic inflammatory pain, and neuropathic pain using I. Although the methods of preparation are not claimed, hundreds of example prepns. and/or characterization data are included. For example, II was prepared in 43% yield from its monooxide III (preparation given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7 are given.

III

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:612064 CAPLUS

DOCUMENT NUMBER: 143:139157

TITLE: Preparation of rigid liposomal cochleate
INVENTOR(S): Krause-Elsmore, Sara L.; Mannino, Raphael J.
PATENT ASSIGNEE(S): Biodelivery Sciences International, Inc., USA

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT	NO.			KIN	D	DATE			APPL	ICAT	ION :	NO.		D.	ATE	
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WO 2005	0632	13		A1		2005	0714		WO 2	004-	US42	927		2	0041	220 <
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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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PRIORITY APPLN. INFO.:

US 2003-531546P P 20031219 <--US 2004-565120P P 20040423

AB Employing liposomes having a high transition temperature at least partially disposed in a matrix, compns. are provided that can be used to deliver one or more cargo moieties, e.g., a drug, a nutrient, an imaging agent and/or nonsteroidal anti-inflammatory drug. The matrix can be a lipid precipitate and/or a cationic bridge. Methods of making and using these compns. preferably cochleates, are also disclosed. Rigid liposomes were obtained from distearoylphosphatidylserine and dextran.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:369133 CAPLUS

DOCUMENT NUMBER: 142:435774

TITLE: Compositions treatment of chronic inflammatory

diseases

INVENTOR(S): Shapiro, Howard K.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S.

Ser. No. 610,073, abandoned.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
				_	
US 20050090553	A1	20050428	US 2004-924945		20040824 <
US 20080234380	A1	20080925	US 2008-70518		20080220 <
PRIORITY APPLN. INFO.:			US 1992-906909	В2	19920630 <
			US 1994-241603	В2	19940511 <
			US 1997-814291	В2	19970310 <
			US 2000-610073	В2	20000705 <
			US 2004-924945	Α2	20040824

OTHER SOURCE(S): MARPAT 142:435774

This invention defines novel compns. that can be used for clin. treatment of a class of chronic inflammatory diseases. Increased generation of carbonyl substances, aldehydes and ketones, occurs at sites of chronic inflammation and is common to the etiologies of all of the clin. disorders addressed herein. Such carbonyl substances are cytotoxic and addnl. serve to perpetuate and disseminate the inflammatory process. This invention defines use of compns., the orally administered required primary agents of which are primary amine derivs. of benzoic acid capable of reacting with the carbonyl substances. P-Aminobenzoic acid (or PABA) is an example of the required primary agent of the present invention. PABA has a small mol. weight, is water soluble, has a primary amine group which reacts with carbonyl-containing substances and is tolerated by the body in relatively high dosages for extended periods. The method of the present invention includes administration of a composition comprising: (1) an orally consumed primary agent; (2) a previously known medicament co-agent recognized as effective to treat a chronic inflammatory disease addressed herein

administered to the mammalian subject via the oral route, other systemic routes of administration or via the topical route; and (3) optionally 1 or more addnl. orally consumed co-agent selected from the group consisting of antioxidants, vitamins, metabolites at risk of depletion, sulfhydryl co-agents, co-agents which may facilitate glutathione activity and nonabsorbable primary amine polymeric co-agents, so as to produce an additive or synergistic physiol. effect of an anti-inflammatory nature.

L8 ANSWER 6 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:999675 CAPLUS

DOCUMENT NUMBER: 141:406127

TITLE: Lamotrigine and related compounds for the

treatment of multiple sclerosis

INVENTOR(S): Harbige, Laurence S.; Leach, Michael J.; Sharief,

Mohammed

PATENT ASSIGNEE(S): BTG International Limited, UK SOURCE: U.S. Pat. Appl. Publ., 4 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040229873 PRIORITY APPLN. INFO.:	A1	20041118	US 2004-756761 GB 2003-783 A	20040114 < 20030114 <
OTHER SOURCE(S): GI	MARPAT	141:406127		

Ι

AB A method of treating a patient in need of therapy for multiple sclerosis is provided, comprising administering a therapeutically ED of I [R1-R5 = H, trihaloalkyl, halo; X1-X3 = CH, CCH2F, CCF3, COalkyl, CCH3, N (with proviso); Y1, Y2 = H, primary amino, secondary amino, tertiary amino] during periods of remission, as well as during relapse. Preferred compds. include e.g. lamotrigine and sipatrigine. The therapy results in reduction of one or more of incidence of relapse, spasticity and fatigue and exceptionally the therapy stabilizes the patients Expanded Disability Status Score (EDSS), thus halting progress of the disease.

L8 ANSWER 7 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2004:902155 CAPLUS

DOCUMENT NUMBER: 141:384286

TITLE: Novel encochleation methods, cochleates and methods of

use

INVENTOR(S):
Mannino, Raphael J.; Gould-Fogerite, Susan;

Krause-Elsmore, Sara L.; Delmarre, David; Lu, Ruying

PATENT ASSIGNEE(S): Biodelivery Sciences International, Inc., USA;

University of Medicine and Dentistry of New Jersey

SOURCE: PCT Int. Appl., 195 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

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			ES,	FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	
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	IIS	2005				A 1		2005	0120		IIS 2	004-	8222	3.0		2	0040	409	<
		1624				A2		2006				004-							
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AB The invention generally relates to cochleate drug delivery vehicles. Disclose are novel methods for making cochleates and cochleate compns. that include introducing a cargo moiety to a liposome in the presence of a solvent. Also disclosed are cochleates and cochleate compns. that include an aggregation inhibitor, and optionally, a cargo moiety. Addnl., anhydrous cochleates that include a protonized cargo moiety, a divalent metal cation and a neg. charge lipid are disclosed. Methods of using the cochleate compns. of the invention, including methods of administration, are also disclosed.

L8 ANSWER 8 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:802560 CAPLUS

DOCUMENT NUMBER: 141:301459

TITLE: Novel formulations and method of treatment

INVENTOR(S):

Buxton, Ian Richard; Currie, Robin; Dela-Cruz, Myrna
A.; Goodson, Gary Wayne; Karolak, Wlodzimierz; Maleki,
Mehran; Iyer, Vijay Mohan; Gopal, Muppirala; Parr,

Alan Frank; Sidhu, Jagdey Singh; Stagner, Robert

Allen; Vijay-Kumar, Akunuri Venkata

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S.

Ser. No. 629,177. CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
				-	
US 20040192690	A1	20040930	US 2003-726752		20031204 <
CN 101229169	A	20080730	CN 2007-10196130		20030728 <
US 20050032799	A1	20050210	US 2003-629177		20030729 <
ZA 2005000518	A	20060726	ZA 2005-518		20050119 <
PRIORITY APPLN. INFO.:			GB 2002-17492	Α	20020729 <
			GB 2002-17493	Α	20020729 <
			GB 2003-13801	Α	20030613 <
			US 2003-629177	A2	20030729 <
			CN 2003-822371	АЗ	20030728 <

AB A sustained release formulation of lamotrigine or a pharmaceutically acceptable derivative thereof and methods of treatment and uses thereof are disclosed.

L8 ANSWER 9 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:633439 CAPLUS

DOCUMENT NUMBER: 141:167771

TITLE: Tetracycline compounds having target therapeutic

activities

INVENTOR(S): Levy, Stuart B.; Draper, Michael; Nelson, Mark L.;

Jones, Graham

PATENT ASSIGNEE(S): Paratek Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 277 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PAT		KINI	D	DATE			APPL	ICAT	ION 1	NO.		D	ATE				
		2004064728 A2 2004064728 A3 W: AE, AG, AL, AM, A							WO 2	004-	US10	36		2	0040	116	<
US PRIORITY	CN GE LK 2006019	CO, GH, LR,	CR, GM, LS,	CU, HR, LT,	CZ, HU, LU,	DE, ID, LV,	DK, IL,	DM, IN, MD,	DZ, IS, MG, US 2 US 2	EC, JP, MK, 004- 003- 001-	EE, KE, MN, 9961 4411	EG, KG, MW, 19 41P 46P	ES, KP, MX,	FI, KR, MZ, 2 P 2 P 2	GB, KZ, NA, 0041 0030 0010	GD, LC, NI 122 116 713	< <
									US 2	002- 002- 004-	1960	10		A2 2	0020 0020 0040	715	-

OTHER SOURCE(S): MARPAT 141:167771

AB Methods and compds. for treating diseases, e.g. inflammation process-associated states, with tetracycline compds. having a target therapeutic activity are described. Preparation of selected tetracycline compds. is described.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 10 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:120727 CAPLUS

DOCUMENT NUMBER: 140:169680

TITLE: Sustained release formulations comprising

lamotrigine

INVENTOR(S): Buxton, Ian Richard; Currie, Robin; Dela-Cruz, Myrna A.; Goodson, Gary Wayne; Karolak, Wlodzimierz; Maleki,

Mehran; Iyer, Vijay Mohan; Muppirala, Gopal; Parr, Alan Frank; Sidhu, Jagdev Singh; Stagner, Robert

Allen; Vijay-kumar, Akunuri Venkata

PATENT ASSIGNEE(S): Glaxo Group Limited, UK; et al.

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PA.	TENT	NO.			KIN	D	DATE			APPL	ICAT	ION :	NO.		D	ATE		
	2004	0127 AE,	41 AG,	AL,	A1 AM,	AT,	2004 AU,	0212 AZ,	BA,	WO 2 BB,	003- BG,	EP83 BR,	68 BY,	BZ,	2 CA,	0030 CH,	728 CN,	
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							RU,								TJ,	TM,	TN,	
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CA	2493		D0 <b>,</b>		A1		2004											<
	2003		36															
	1524						2005											
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙΤ,	LI,	LU,	NL,	SE,	MC,	PT,	
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BR	2003	0131	48		Α		2005	0712		BR 2	003-	1314	8		2	0030	728	<
CN	1681	509			А		2005			CN 2	003-	8223	71		2	0030	728	<
CN	1681 1003 2005 5378 2325	6300	7		С		2008								_			
JP	2005	5381	13		Τ		2005					5253						
NZ	5378	85			A		2007					5378						
RU	2325 1012	163	_		C2		2008					1053						
	2005						2008 2006			CN Z	00/-	1019 518	6130		2	0030	110	<
	2005				A		2006					1243						
	8827		40		B1		2009					7016						
	2005						2005					948						
	2007						2007					2022						
	Y APP									GB 2	002-	1749	2		A 2	0020	729	<
												1749						
												1380				0030		
												2603						
												8223						
					_							EP83				0030		<
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its derivative for treatment of CNS disorder comprises (by weight) 2.5 to 80% lamotrigine or its derivative, 10 to 70% release retarding polymer, 0to 70% diluent, 0 to 20% compression aid, and 0.1 to 2.5% lubricant. Substantially all the lamotrigine or a pharmaceutically acceptable derivative is released from the formulation in a period of  $2\ \text{to}\ 20$ h after administration to a patient, producing an Area Under the Curve

value of 80 to 125% and Cmax of about 30% less than that of an instant-release tablet containing the same amount of lamotrigine. For example, a tablet formulation (Diffcore device) was prepared comprising (i) a core containing lamotrigine 200 mg, a blend of hydroxypropyl Me celluloses K100LV 62.64 mg and E4M 45.36 mg, lactose monohydrate 90.4 mg, and magnesium stearate 1.6 mg, and (ii) an outer coat containing Eudragit L30 D-55 (30% weight/weight solution) 17.3 mg, Red Iron Oxide 0.37 mg, tri-Et

 $1.81~\mathrm{mg}$ , glyceryl monostearate  $0.494~\mathrm{mg}$ , and Polysorbate  $80~0.02~\mathrm{mg}$ . The coating included orifices allowing the release of lamotrigine from the core.

# => d 11-20 L8 ibib abs

L8 ANSWER 11 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:319381 CAPLUS

DOCUMENT NUMBER: 138:334051

TITLE: Diagnostic methods for determining susceptibility to

convulsive conditions

INVENTOR(S): Campbell, Allyson J.; Weaver, Donald F.; Lyon, Angela

P.; Carran, John R.

PATENT ASSIGNEE(S): Queen's University At Kingston, Can.

SOURCE: U.S. Pat. Appl. Publ., 14 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20030077833	A1	20030424	US 2002-222957	_	20020816 <
CA 2399169	A1	20030307	CA 2002-2399169		20020816 <
US 20060008917	A1	20060112	US 2005-106369		20050413 <
US 7153692	В2	20061226			
US 20070042497	A1	20070222	US 2006-586781		20061026 <
PRIORITY APPLN. INFO.:			US 2001-318139P	Р	20010907 <
			US 2002-378781P	Р	20020507 <
			US 2002-222957	В1	20020816 <
			US 2005-106369	Α1	20050413

AB The present invention exploits the discovery that amts. of uracil and thymine metabolites, especially  $\beta$ -aminoisobutyric acid, in various bodily fluids, especially urine, are correlated with the occurrence of epilepsy when compared to matched control subjects. Anal. and diagnostic protocols, including a novel high performance liquid chromatog. system, for use in the invention are disclosed.

L8 ANSWER 12 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:319348 CAPLUS

DOCUMENT NUMBER: 138:331688

TITLE: Methods of suppressing microglial activation and

systemic inflammatory responses

INVENTOR(S): Laskowitz, Daniel T.; Matthew, William D.; McMillian,

Michael

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S.

Ser. No. 957,909.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

### PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
				_	
US 20030077641	A1	20030424	US 2002-252120		20020923 <
US 20020164789	A1	20021107	US 2001-957909		20010921 <
US 7205280	В2	20070417			
PRIORITY APPLN. INFO.:			US 1998-77551P	P	19980311 <
			US 1999-260430	В2	19990301 <
			US 2001-957909	A2	20010921 <

AB Methods of suppressing the activation of microglial cells in the Central Nervous System (CNS), methods of ameliorating or treating the neurol. effects of cerebral ischemia or cerebral inflammation, and methods of combating specific diseases that affect the CNS by administering a compound that binds to microglial receptors and prevents or reduces microglial activation are described. ApoE receptor binding peptides that may be used in the methods of the invention are also described, as are methods of using such peptides to treat peripheral inflammatory conditions such as sepsis. Also described are methods of screening compds. for the ability to suppress or reduce microglial activation. Injection of ApoE (133-149) in mice suppressed serum levels of TNF $\alpha$  and IL-6 following LPS administration.

L8 ANSWER 13 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:154224 CAPLUS

DOCUMENT NUMBER: 138:193294

TITLE: Expandable gastric retention device containing

pharmaceutical compositions

INVENTOR(S): Ayres, James W.

PATENT ASSIGNEE(S): The State of Oregon Acting by and Through the State

Board of Higher Education On Behalf of Oregon State

University, USA

SOURCE: PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PA:	rent	NO.			KIN	D	DATE			APPL	ICAT	ION :	NO.		D	ATE		
WO	2003	0157	45		A1	_	2003	0227		WO 2	001-	US46	146		2	0011	022 ·	<
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		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,	
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	KΖ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MΖ,	NO,	NΖ,	PH,	PL,	
		PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	
		US,	UZ,	VN,	YU,	ZA,	ZW											
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,	
		DE,	DK,	ES,	FΙ,	FR,	GB,	GR,	ΙE,	ΙΤ,	LU,	MC,	ΝL,	PT,	SE,	TR,	BF,	
		ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	ΤG		
CA	2456	976			A1		2003	0227		CA 2	001-	2456	976		2	0011	022 -	<
ΑU	2002	2258	72		A1		2003	0303	,	AU 2	002-	2258	72		2	0011	022 -	<
EΡ	1416	914			A1		2004	0512		EP 2	001-	9953	28		2	0011	022 -	<
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙΤ,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,	FΙ,	RO,	MK,	CY,	AL,	TR							
BR	2001	0171	23		Α		2004	0928		BR 2	001-	1712	3		2	0011	022 -	<
CN	1543	337			A		2004	1103		CN 2	001-	8235	44		2	0011	022 -	<
JΡ	2005	5010	97		T		2005	0113								0011	022 -	<
NZ	5314	61			А		2008	0328		NZ 2	001-	5314	61		2	0011	022 -	<
ИО	2004	0006	11		A		2004	0416		NO 2	004 -	611			2	0040	211 ·	<
MX	2004	0013	88		А		2004	0527		MX 2	004-	1388			2	0040	213 -	<

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US 20040219186 A1 20041104 US 2004-778917 20040213 <--
IN 2004KN00232 A 20051230 IN 2004-KN232 20040219 <--
ZA 2004002066 A 20050509 ZA 2004-2066 20040315 <--
PRIORITY APPLN. INFO.:

US 2001-313078P P 20010816 <--
WO 2001-US46146 W 20011022 <--
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AB The present application concerns gastric retention devices formed from compns. comprising polymeric materials, such as polysaccharides, and optional addnl. materials including excipients, therapeutics, and diagnostics, that reside in the stomach for a controlled and prolonged period of time. Dry powders of xanthan gum and locust bean gum were mixed intimately were converted to dried films. The dried films were compressed with the help of specially made punches and dies. A series of dies with decreasingly narrow internal diams. were used. A punch pushes the film from one die into the next die, followed by pushing of the film by another punch into the next die. This process takes place in succession until a point is reached where the film is small enough to put into a desired capsule size.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:57866 CAPLUS

DOCUMENT NUMBER: 138:117673

TITLE: Tetracycline compounds having target therapeutic

activities

INVENTOR(S): Levy, Stuart B.; Draper, Michael; Nelson, Mark L.;

Jones, Graham

PATENT ASSIGNEE(S): Paratek Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 158 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

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PATENT NO.
                      KIND DATE APPLICATION NO. DATE
                                  _____
                                                 _____
     WO 2003005971
                           ____
                           A2 20030123
A3 20031127
                                                WO 2002-US22451
                                                                           20020715 <--
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
              UA, UG, UZ, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
              KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
              FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
              CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2002318238
                            A1 20030129 AU 2002-318238
                                                                            20020715 <--
                                                US 2002-196010
                                                                            20020715 <--
     US 20040063674
                            Α1
                                    20040401
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                            A2
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          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     JP 2004537544 T
US 20060194773 A1
                                                 JP 2003-511780
                                    20041216
                                                                            20020715 <--
                            A1
                                   20060831
                                                 US 2004-996119
                                                                            20041122 <--
                                                 US 2004-996119 20041122 <--
US 2001-305546P P 20010713 <--
US 2002-395741P P 20020712 <--
US 2002-196010 A2 20020715 <--
WO 2002-US22451 W 20020715 <--
US 2003-441141P P 20030116 <--
US 2004-759484 B1 20040116
PRIORITY APPLN. INFO.:
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OTHER SOURCE(S): MARPAT 138:117673

Methods and compds. for treating a variety of diseases with tetracycline compds. having a target therapeutic activity are described, as is compound

preparation

3 REFERENCE COUNT: THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 15 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN 1.8

ACCESSION NUMBER: 2002:964194 CAPLUS

DOCUMENT NUMBER: 138:33355

TITLE: Treating nerve pain by targeting

hyperpolarization-activated, cyclic nucleotide-gated

channels (HCN)

Chaplan, Sandra; Dubin, Adrienne; Lee, Doo Hyun; Liu, INVENTOR(S):

Changlu

PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA; The Regents of

the University of California

PCT Int. Appl., 133 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

		TENT				KIND DATE					ICAT								
	WO	2002	1004	08				2002	1219						20020530 <				
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								NL, NE,				BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	
	ΑU		027 3057	38	·	A1 A1	ŕ	2002 2002	1219 1223		CA 2			20020530 < 20020530 <					
	US US	2003	0022 0022	812 813		A1 A1	2003 2003	0130 0130	US 2002-158684 US 2002-158711 EP 2002-734581						20020530 <				
		R:		BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,							
			5168	88		Τ		2005	0609	CY, AL, TR JP 2003-503229 MX 2003-11331									
PRIO		Y APP									US 2 US 2 US 2	001- 001- 002-	2971 3479 3730	08P 45P 12P		P 2 P 2 P 2	0011	107 416	<
AB	WO 2002-US16910 Markedly enhanced activity of pacemaker (hyperpolarization																		

Markedly enhanced activity of pacemaker (hyperpolarization-activated, cation-nonselective, HCN) ion channels governs spontaneous firing in sensory cells of allodynic rats. An HCN ion channel specific blocker, ZD7288, dose-dependently and completely suppresses allodynia. Nerve injury increases the population of large DRG neurons expressing a high d. of Ih and modulates HCN mRNA expression. New methods of treating pain by targeting HCN pacemaker channels are developed. In addition, new methods for identifying compns. useful for treating pain are disclosed.

ACCESSION NUMBER: 2001:168179 CAPLUS

DOCUMENT NUMBER: 134:204759

TITLE: Screening for axon viability using substance capable of stimulating soluble guanylate cyclase and screening

for agents protecting axons

Garthwaite, Giti; Garthwaite, John INVENTOR(S):

PATENT ASSIGNEE(S): University College London, UK

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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		1016359							WO 2000-GB3360						20000831 <					
WO		001016359																		
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		HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	KΡ,	KR,	KΖ,	LC,	LK,	LR,	LS,	LT,			
		LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,			
		SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,			
		YU,	ZA,	ZW																
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		DE,	DK,	ES,	FΙ,	FR,	GB,	GR,	ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,			
		CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG						
GB	3 2370636				A 2002070				GB 2002-7441							20000831 <				
EP	1220945				A2 20020710					EP 2000-956708						20000831 <				
	R:	AT,	BE,	CH,	DE.	DK.	ES,	FR.	GB,	GR,	IT.	LI.	LU.	NL.	SE,	MC.	PT,			
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determining thereby whether the axon is viable. Nitric oxide, YC-1, or carbon monoxide are used to stimulate sGC and cGMP is determined

ANSWER 17 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:634698 CAPLUS

DOCUMENT NUMBER: 134:125828

TITLE: Low-dose gabapentin combined with either lamotrigine or carbamazepine can be useful therapies for trigeminal neuralgia in multiple

sclerosis

Solaro, C.; Uccelli, M. Messmer; Uccelli, A.; Leandri, AUTHOR(S):

M.; Mancardi, G. L.

Department of Neurological Sciences and CORPORATE SOURCE:

Rehabilitation, University of Genoa, Genoa, I-16132,

Italy

SOURCE: European Neurology (2000), 44(1), 45-48

CODEN: EUNEAP; ISSN: 0014-3022

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal LANGUAGE: English

Paroxysmal symptoms occur frequently in multiple sclerosis (MS). Usually they are treated with carbamazepine (CBZ) and phenytoin, although these medications are often interrupted due to adverse effects. We report 11 MS patients with trigeminal neuralgia (TN): 6 intolerant to a therapeutic dosage of CBZ, showing serious adverse

effects and subsequently treated with a combination of low-dose CBZ and gabapentin (GBP) (group 1); 5 treated with lamotrigine (LMT), showing adverse effects and subsequently treated with GBP (group 2). Subjective pain level and impairment in performing daily activities were rated utilizing a 3-point scale at time 0 and at optimal dosage time (T1). GBP was initiated at 300 mg daily and titrated, until pain control was achieved without new adverse effects, to a maximum dose of 1,200 mg daily. CBZ or LMT were reduced to a level which no longer produced adverse effects, although resulting in a lack of efficacy in relieving pain. Pain control was obtained in all patients but 1, with no side effects. The plasma level anal., performed in 5 patients, resulted in normal values. The mean dosages at T1 were: group 1 CBZ 400 mg and GBP 850 mg daily; group 2 LMT 150 mg and GBP 780 mg daily. Combining drugs with complementary modes of action may provide a rational pharmacol. approach to the management of TN in MS.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:451524 CAPLUS

DOCUMENT NUMBER: 127:117323

ORIGINAL REFERENCE NO.: 127:22493a,22496a

TITLE: Clinical effectiveness of lamotrigine and

plasma levels in essential and symptomatic trigeminal

neuralgia

AUTHOR(S): Lundardi, Gianluigi; Leandri, Massimo; Albano,

Claudio; Cultrera, Serena; Fracassi, Maurizio; Rubino,

Vitatonio; Favale, Emilio

CORPORATE SOURCE: Department of Neuroscience and Centro

Interuniversitario per la Neurofisiologia del Dolore,

University of Genoa, Italy

SOURCE: Neurology (1997), 48(6), 1714-1717

CODEN: NEURAI; ISSN: 0028-3878

PUBLISHER: Lippincott-Raven

DOCUMENT TYPE: Journal LANGUAGE: English

AB This paper reports on the effectiveness of oral lamotrigine in 15 patients suffering from "essential" trigeminal neuralgia and in five patients suffering symptomatic trigeminal neuralgia concomitant with multiple sclerosis. We recorded objective and subjective pain ratings and correlated them to daily dosage (400 mg maximum) and plasma levels of the drug. We detected pain relief proportional to daily dosage and to drug plasma levels. Eleven of the cases affected by the "essential" form of neuralgia showed complete pain relief on reaching their maximum daily dosage. All cases affected by the symptomatic form had complete pain relief. We could detect no changes from these results by the end of the follow-up period (3 to 8 mo after the study ended).

L8 ANSWER 19 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:137849 CAPLUS

DOCUMENT NUMBER: 126:166012

ORIGINAL REFERENCE NO.: 126:31932h,31933a

TITLE: Trigeminal neuralgia. A guide to drug choice

AUTHOR(S): Cheshire, William P.

CORPORATE SOURCE: Department of Neurology, Mayo Clinic Jacksonville,

Jacksonville, FL, USA

SOURCE: CNS Drugs (1997), 7(2), 98-110 CODEN: CNDREF; ISSN: 1172-7047

PUBLISHER: Adis

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 93 refs. Trigeminal neuralgia, also known as tic

douloureux, is an idiopathic condition of severe, unilateral, paroxysmal facial pain. The abrupt nature of the painful attacks (a temporal profile that is similar to that of seizures) led to the discovery that some anticonvulsant drugs are effective against neuralgia. Carbamazepine is the drug of choice, and treatment requires careful dosage titration Baclofen, phenytoin and sodium valproate are also effective. Transient relief is sometimes possible with local anesthetics. Limited data suggest that topical capsaicin, and tizanidine, lamotrigine, oxcarbazepine, pyridostigmine and enalapril have helped some patients. While effective, other drugs are limited by their adverse effects; for example, clonazepam is too sedating, pimozide induces extrapyramidal adverse effects, and tocainide and felbamate can cause aplastic anemia. Phenobarbital (phenobarbitone), opioids, mexiletine, tricyclic antidepressants, corticosteroids, nonsteroidal anti-inflammatory drugs and sympatholytics are ineffective. The antineuralgic effect of any drug may eventually wear off. If this occurs, combination therapy can restore pain relief, as can the reintroduction of a previously effective drug following a drug-free interval. Similar pharmacol. strategies potentially apply to other paroxysmal pain syndromes such as vagoglossopharyngeal neuralgia. Clin. overlap with multiple sclerosis or cluster headache suggests addnl. drugs that may be useful in specific patients. Effective neurosurgical procedures exist for patients with trigeminal neuralgia that is refractory to medications.

ANSWER 20 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1996:94551 CAPLUS

DOCUMENT NUMBER: 124:194132

ORIGINAL REFERENCE NO.: 124:35639a,35642a

TITLE: The effects of anticonvulsants on

4-aminopyridine-induced bursting: in vitro studies on

rat peripheral nerve and dorsal roots

AUTHOR(S): Lees, G.

CORPORATE SOURCE: Dep. Academic Anaesthetics, Imperial College Medicine,

London, W2 1NY, UK

SOURCE: British Journal of Pharmacology (1996),

117(3), 573-9

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aminopyridines have been used as beneficial symptomatic treatments in a variety of neurol. conditions including multiple sclerosis but have been associated with considerable toxicity in the form of abdominal pain, paraesthesias and (rarely) convulsions. Extracellular and intracellular recording was used to characterize action potentials in rat sciatic nerves and dorsal roots and the effects of 4-aminopyridine (4-AP). In sciatic nerve trunks, 1 mM 4-AP produced pronounced after potentials at room temperature secondary to regenerative firing

in affected axons (5-10 spikes per stimulus). At physiol. temps., after potentials (2-3 spikes) were greatly attenuated in peripheral axons. 4-AP evoked more pronounced and prolonged after discharges in isolated dorsal roots at 37°C (3-5.5 mV and 80-100 ms succeeded by a smaller inhibitory/depolarizing voltage shift) which were used to assess the effects of anticonvulsants. Phenytoin, carbamazepine and lamotrigine dose-dependently reduced the area of 4-AP-induced after potentials at 100 and 320  $\mu\text{M}$  but the amplitude of compound action potentials (evoked at 0.5 Hz) was depresed in parallel. The tonic block of sensory action potentials by all three drugs (at 320  $\mu\text{M}$ ) was enhanced by high frequency stimulation (5-500 Hz). The lack of selectivity of these frequency-dependent Na+ channel blockers for burst firing, compared to low-frequency spikes, is discussed in contrast to

their effects on 4-AP-induced seizures and paroxysmal activity in CNS tissue (which is associated with large and sustained depolarizing plateau potentials). In conclusion, these in vitro results confirm the marked sensitivity of sensory axons to 4-AP (the presumptive basis for paraesthesias). Burst firing was not preferentially impaired at relatively high concns. suggesting that anticonvulsants will not overcome the toxic peripheral actions of 4-AP in neurol. patients.

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